This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

See reverse side for additional information.

Interagency Report Control No 0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

# ANNUAL REPORT OF RESEARCH FACILITY
*(TYPE OR PRINT)*

**1. REGISTRATION NO.** 48-R-0004 **CUSTOMER NO.** 1400

FORM APPROVED
OMB NO. 0579-0036

**2. HEADQUARTERS RESEARCH FACILITY** *(Name and Address, as registered with USDA, include Zip Code)*

BAYER CORP. AGRIC. DIVISION, TOXICOLOGY
BAYER RESEARCH PARK
(b)(2)High, (b)(7)(F)
STILWELL, KS 66085
(913) 433-5221 (913)433-5100

**3. REPORTING FACILITY** (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

**FACILITY LOCATIONS** *(sites)*

See Attached Listing

**REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY** *(Attach additional sheets if necessary or use APHIS FORM 7023A )*

| A. Animals Covered By The Animal Welfare Regulations | B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes. | C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs. | D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used. | E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report)* | F. TOTAL NO. OF ANIMALS (Cols. C + D + E) |
|---|---|---|---|---|---|
| 4. Dogs | 36 | 506 | 1 | 2 | 509 |
| 5. Cats | | 0 | | | 0 |
| 6. Guinea Pigs | | 0 | | | 0 |
| 7. Hamsters | | 0 | | | 0 |
| 8. Rabbits | | 0 | | | 0 |
| 9. Non-Human Primates | 1 | 36 | 36 | | 72 |
| 10. Sheep | | 0 | | | 0 |
| 11. Pigs | | 0 | | | 0 |
| 12. Other Farm Animals | | 0 | | | 0 |
| | | | | | |
| 13. Other Animals | | 0 | | | 0 |
| | | | | | |
| | | | | | |
| | | | | | |

**ASSURANCE STATEMENTS**

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all the exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

**CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL**
**(Chief Executive Officer or Legally Responsible Institutional official)**
I certify that the above is true, correct, and complete (7 U.S.C. Section 2143)

**SIGNATURE** (b)(6),(b)(7)(c) **NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL** *(Type or Print)* (b)(6),(b)(7)(c) **DATE SIGNED** 11-9-06

**APHIS FO** [redacted] **t 88), which is obsolete** **PART 1 - HEADQUARTERS**
**(AUG 91)**

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48R0004

## Column E Explanation

1. **Registration Number**: 48-R-0004

2. **Number of animals used in this study:** 1

3. **Species (common name) of animals used in this study:** Dog

4. **Explain the procedure producing pain and/or distress:**

   A single dose toxicity study was conducted in which no adverse effects were anticipated at the doses administered, based on the results of a previous study. However, just after dosing, one dog exhibited reddened ears and dilated pupils, felt hot to the touch, vomited, had difficulty breathing, and died within a few minutes

5. **Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)**

   A veterinarian was present at the time of dosing, but the sequence of events occurred too quickly to intervene with treatment.

6. **What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102)**

   FDA, 21 CFR 312.23 (a) (8) (ii): IND content and format; Pharmacology and toxicology information; Toxicology. Requires "an integrated summary of the toxicological effects of the drug in animals..." and "....the description is to include the results of acute, subacute and chronic toxicity tests...".

   CDER Guidance for Industry Single Dose Acute Toxicity Testing for Pharmaceuticals (Aug 1996). III Testing Procedures: "The test compound should be administered to animals to identify doses causing no adverse effect and doses causing major (life-threatening) toxicity.

**Agency:** Food and Drug Administration **CFR:** 21 CFR 312.23 (a)(8)(ii)

48R0004

## Column E Explanation

1. **Registration Number**: 48-R-0004

2. **Number of animals used in this study:** 1

3. **Species (common name) of animals used in this study:** Dog

4. **Explain the procedure producing pain and/or distress:**

   A pilot (maximum tolerated single dose) toxicity study was conducted to determine doses for subsequent studies. One dog experienced a brief seizure after dosing.

5. **Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)**

   The drug administered in this study is a potential pharmaceutical candidate for human use. To determine adequate safety of the drug in humans, elevated pharmacological doses are required to be administered to animals in pre-clinical studies. The pharmacologic signs associated with the drug cannot be treated since the objective is to determine safety and/or reversibility of the compound.

6. **What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102)**

   FDA, 21 CFR 312.23 (a) (8) (ii): IND content and format; Pharmacology and toxicology information; Toxicology. Requires "an integrated summary of the toxicological effects of the drug in animals..." and "....the description is to include the results of acute, subacute and chronic toxicity tests...".

   CDER Guidance for Industry - Single Dose Acute Toxicity Testing for Pharmaceuticals (Aug 1996). III Testing Procedures: "The test compound should be administered to animals to identify doses causing no adverse effect and doses causing major (life-threatening) toxicity".

**Agency:** Food and Drug Administration **CFR:** 21 CFR 312.23 (a)(8)(ii)



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